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THE FIRST QUARTERLY REPORT

OF THE

MICHIGAN STATE LABORATORY OF HYGIENE

By PROF. VICTOR C. VAUGHAN, M. D., Ph. D.,
Member of the State Board of Health, and Director of the Laboratory of Hygien

[Reprinted from the Annual Report of the Michigan State Board of Health, for the Year 1887.]

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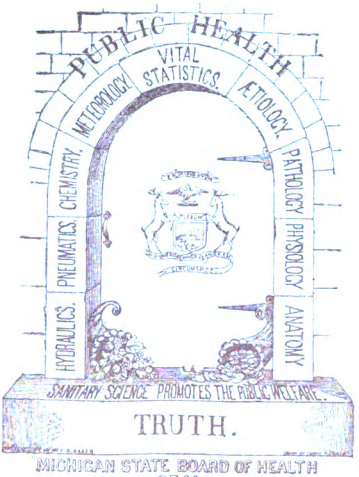

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To the Michigan State Board of Health:

GENTLEMEN: In accordance with the recommendation made by you at your meeting in October, 1886, the Regents of the State University asked the Legislature for an appropriation to build and equip a laboratory of practical hygiene in which original investigations as to the causation and nature of diseases might be made. A portion of the amount asked was granted by the Legislature, and in June, 1887, the Regents established a department of hygiene, appointed the undersigned director of the laboratory and professor of hygiene, and Frederick G. Novy instructor in hygiene. The laboratory building is now in process of erection, and will be ready for occupancy in October, 1888. However, last October, Mr. Novy and I began our work, using rooms and apparatus belonging to the chemical laboratory. The first few weeks were spent in investigating the fatal cases of milk-poisoning, which occurred near Milan. The mystery connected with these cases was cleared up, unjust accusations were hushed, and the great care necessary to prevent milk-poisoning was emphasized. Later, Mr. Novy's investigations showed the fraud being practiced upon the people in the so-called new local anæsthetic, stenocarpine. The exposure of this fraud was so complete that the mixture has been withdrawn from the market.

The greater part of the quarter's work has been given to the investigation of the epidemic of typhoid fever at Iron Mountain. If this work will cause people to give more attention to the purity of their drinking water, many lives will be saved. Reports of these investigations are herewith submitted to you. Besides the above, we have made analyses of water, with the view of selecting a source of public supply at Albion.

Respectfully,

VICTOR C. VAUGHAN,

Director of the Michigan State Laboratory of Hygiene.

EXPERIMENTAL STUDIES ON THE CAUSATION OF TYPHOID FEVER WITH SPECIAL REFERENCE TO THE OUTBREAK AT IRON MOUNTAIN, MICH.—PRELIMINARY REPORT.*

BY VICTOR C. VAUGHAN, M D., PH. D., AND FREDERICK G. NOVY, M. S.

Last October, having heard of the prevalence of a severe epidemic of typhoid fever at Iron Mountain, Michigan, we requested Dr. G. B. Johnson, a physician of that place, to forward to us a sample of the drinking water, used by families in which the disease had appeared. This request was immediately complied with, and we determined to make the most thorough tests possible. The ordinary sanitary analysis, which consists in the determination of free and albuminoid ammonia, chlorine, nitrates and nitrites, we determined would be altogether inadequate. Besides, as we afterwards learned, such an analysis had already been made by the competent chemists of the Chapin mine at Iron Mountain. The results of this analysis, together with those of other waters in the village, made by the same chemists, will be given further on.

After much deliberation we determined to inoculate sterilized meat preparations and sterilized milk with the suspected water, and then to keep the material at or near the temperature of the human body for varying periods of time, and to ascertain whether or not there would be any poisons developed by the bacteria, which were suspected of being in the water. The following are the details of the method: A number of Erlenmeyer flasks of 400 c. c. capacify were thoroughly cleansed and rinsed with distilled water; then dried in an air-bath. When dry, they were tightly closed with plugs of cotton and heated for two hours at 140–150°C.

A litre of fresh milk was placed in a large flask, plugged with cotton, and heated in a Koch's steam sterilizing apparatus for over three hours. The flask was then taken out and, while yet warm, its contents were transferred by means of a sterilized graduate and sterilized funnel, in portions of 150 c. c. each, to the above mentioned sterilized, small flasks. The transfer was made as speedily as possible and the flasks were immediately plugged with cotton and capped with pieces of filter-paper, which were held in position by means of rubber bands. The flasks, thus prepared, were placed in the steam sterilizing apparatus and heated for two hours. This was found to produce perfect sterilization.

*This is part of the First Quarterly Report to the State Board of Health, of work done in the Michigan State Laboratory of Hygiene, at the State University.

One pound of lean beef was chopped up finely and treated with one litre of distilled water. The whole was set aside in a cool place for twenty-four hours, being occasionally well shaken. It was then filtered through cloth, the filtrate was diluted to one litre with distilled water, placed in a large beaker and heated almost to boiling. Then twenty-one grams of peptone and five grams of pure sodium chloride were added. While still hot, the solution was carefully neutralized with sodium carbonate, then placed in the steam sterilizer and heated for two and one-half hours. After removal and when nearly cold it was filtered through paper; the filtrate was made up to one litre with distilled water, placed in a large assay flask, plugged with cotton, and heated in the steam sterilizer for three hours. After cooling it was transferred to the sterilized flasks, which were plugged with cotton and heated for two hours in the steam sterilizer.

November 9, 3 P. M., some of these flasks were inoculated with Iron Mountain water; others with some water which we had received from Lansing, Mich., and which had been used by a family, some members of which suffered from typhoid fever; and one each of the milk and meat preparation was left without inoculation and used as controls.

Two of the meat and two of the milk flasks were inoculated with 30 c. c. each of the Iron Mountain water, and one meat and one milk flask with 50 c. c. each of the same water. The same number of flasks and the same amount of water were used with the Lansing water. Thus we had six flasks inoculated with the Iron Mountain water, six with the Lansing water, and two controls.

These flasks were then placed in a Koch's vegetation apparatus and kept at from 30°–38°c.

Nov. 11, 47½ hours after the inoculations were made, four flasks, one containing meat preparation and Iron Mountain water, the second, milk and Iron Mountain water, the third, meat preparation and Lansing water, and the fourth, milk and Lansing water, were removed from the vegetation trough and examined.

The meat preparation inoculated with Iron Mountain water had a strong, repulsive odor, showed an abundant, white bacterial growth, and was neutral in reaction. It was filtered, rendered feebly acid with hydrochloric acid, extracted with ether, then rendered alkaline with sodium carbonate, and extracted successively with ether, benzole and amylic alcohol.

The acid ether extract was allowed to evaporate spontaneously, the residue was dissolved in alcohol, acidulated with dilute hydrochloric acid and evaporated on the water bath. The reddish residue was dissolved in water, filtered and tested for ptomaines. It gave no alkaloidal reactions and contained no poison.

The alkaline ether extract, treated in the same manner as the acid extract, gave slight precipitates with phosphomolybdic acid and platinum chloride, but was also inert.

The alkaline benzole extract gave no alkaloidal reaction and was free from poisonous properties.

The amylic alcohol extract gave slight precipitates, but if it contained any poison the amount was too small to have any effect upon animals.

After the above extractions had been made, the fluid was again rendered acid with dilute hydrochloric acid, and then evaporated in vacuo at 40°C. The residue was treated with absolute alcohol, filtered and again evaporated

in vacuo, again taken up with absolute alcohol and now allowed to evaporate spontaneously. The final residue dissolved in water gave precipitates with many of the alkaloidal reagents, but showed no poisonous properties.

We were now convinced that no poison had yet developed in the meat preparation inoculated with the Iron Mountain water.

Similar examinations were made with the milk and Iron Mountain water, the meat preparation and Lansing water and the milk and Lansing water, and similar results, so far at least as the failure to detect any poison is concerned, were marked. Indeed, the chemical reactions were reached by only slight variations. The bacterial growths were much more abundant in the Iron Mountain water inoculations than in the others.

Nov. 16, seven days after the inoculations were made, four flasks, similar to those previously examined, were removed from the vegetation apparatus, and their contents were submitted to analyses similar to those already detailed.

The meat preparation inoculated with the Iron Mountain water was strongly alkaline in reaction and gave off a marked amine odor. After being acidified with hydrochloric acid, it was evaporated on the water-bath, the residue was extracted with absolute alcohol and filtered. The filtrate gave a precipitate with an alcoholic solution of mercuric chloride, but the precipitate proved readily soluble in slight excess of the precipitant. The mercury was removed by precipitation with hydrogen sulphide and filtration. The filtrate was evaporated on a water-bath, leaving a syrupy residue with some crystals of sodium chloride. The syrup was poured off from the crystals, taken up with water, and a portion of it (only a few drops of the syrup) was injected by means of a hypodermic syringe under the skin on the back of a cat. The temperature of the cat before the injection, taken with care and with a tested thermometer in the axilla, was 99.5°. The following is a record of the effect observed in the experiment:

Experiment 1.—Temperature before the injection, 99.5°

Time of injection, 3:14.

Temperature at 3:24, 100.25.

Temperature at 3:44, 101°. The cat drinks a large quantity of water, although she had an abundant supply of milk, which had been within her reach during the day and of which she had previousiy partaken. After drinking there is considerable retching, but no vomiting. The respirations are greatly accelerated and jerky. The pupils are dilated, but respond to light.

Temperature at 3:54, 101.8°.

Temperature at 4:19, 101.8°.

Temperature at 4:30, 101.5°.

The temperature was not again taken until the next morning, when it was found to be 99.5°. The animal seemed to have wholly recovered from any discomfort which it had suffered.

Experiment 2.—Two days later a similar amount of the syrupy residue was administered to the same cat in the same manner.

Temperature before the injection, 99.5°.

Time of injection, 4:30.

Temperature at 5:00, 102.0°.

The temperature was not taken again until next morning when it was found to be 99.5°.

Experiment 3.—A similar amount of the syrup was administered to another cat.

Temperature before the injection, 100°.
Time of injection, 3:33.
Temperature at 4:08, 101°.
Temperature at 4:33, 101°.
Temperature at 4:50, 101.6°.

Experiment 4.—Dec. 1. A much larger amount of the syrup than that used in the preceding experiments was injected under the skin on the back of a large Maltese cat.

Temperature before the injection, 99.5°.
Time of injection, 4:03 P. M.
Temperature at 4:19 P. M., 94°—marked salivation.
Temperature at 4:44 P. M., 98°—pupils are widely dilated. The cat vomits heavily and persistently.
Temperature at 5:30 P. M., 100°. The retching continues and a watery secretion flows from the mouth, nose and eyes.
Temperature at 6:00 P. M., 100°. Seems in a stupor.
Temperature at 8:00 A. M., Dec. 2, 103.4°. Stupor continues.
Temperature at 1:40 P. M., Dec. 2, 103.4°. When touched on the abdomen the animal cries as if in pain.
Temperature at 4:20 P. M., 104.1°. The animal seems much excited and dashed through the door of the room once, though she had previously been very quiet.
Temperature at 9:15 A. M., Dec. 3, 99.6°. Seems to be recovering, but still looks very haggard. Has eaten nothing since the injection.
Temperature at 1:40 P. M., Dec. 3, 100.8°. Eats some meat.
Temperature at 8:50 A. M., Dec. 4, 99.5°.

The cat was now killed with chloroform and careful examination made of the abdominal and thoracic organs. No abnormality could be found.

Experiment 5.—Some of the syrup obtained from the milk which was inoculated with Iron Mountain water was injected under the skin on the back of cat. The temperature in this case was taken in the rectum.

Temperature before the injection, 102.5°.
Time of the injection, 3:55 P. M., Dec. 9.
Temperature at 4:40 P. M., 97.6°.
Temerature at 5:25 P. M., 100.9°.
Temperature at 9:05 A. M., Dec. 10, 103.6°.
Temperature at 2:40 P. M., Dec. 10, 102.4°.

Both the meat preparation and the milk, which had been inoculated with the Lansing water, were carried through the same chemical processes to which the Iron Mountain preparation had been submitted, but they yielded only traces of the syrupy residue and these when injected into animals were without effect. These served as controls for the experiments already detailed and showed that there was nothing in the meat preparation or milk themselves which could cause the effects observed. As further control, however, the sterilized meat preparation which had been prepared as a control and which had remained in the vegetation trough for forty days at the temperature of the body without showing any bacterial growth was treated in the same manner that the other preparations had been, and the alcoholic residue was injected into animals without producing any effect.

Evidently the syrupy residue, which was used in the above experiments, contains a poisonous ptomaine, the special or characteristic production of

the micro-organisms present in the Iron Mountain water; and if these are the germs of typhoid fever, this syrup contains the special poison of typhoid fever. In the intestines of a man suffering from typhoid fever, the germs grow and constantly produce the ptomaine which is absorbed and causes the symptoms of the disease. If our extract contains the typhoid fever poison, we should expect it to produce, when employed as in the above experiment, in general the symptoms of the disease, but we should expect these symptoms to be temporary. We think that this is substantially what is shown by the experiments. The primary depression of temperature observed when the larger amounts were employed is certainly nothing more than might be expected from a large dose of a powerful poison; then the elevation of temperature which followed was in the majority of the experiments at least sufficiently marked. We did not expect to find in the animal examined the characteristic intestinal lesions of typhoid fever, as we suppose these to be due to the growth and activity of the micro-organism or to the local action of the ptomaine where it exists in larger amount, the place of its formation.

In 1885, Brieger [1] of Berlin, obtained from pure cultures of the Eberth bacillus, a ptomaine which in guinea-pigs produced a slight flow of saliva, frequency of respiration, dilatation of the pupils, profuse diarrhœa, paralysis and death within from twenty-four to forty-eight hours. Post mortem examination showed the heart in systole, the lungs hyperæmic, and the intestines contracted and pale. This substance Brieger considers the special poison of typhoid fever, and calls it typhotoxine, and it may be that we shall find that it forms the active principle of our syrupy residue. At present, however, the two do not seem to be identical. Brieger found no elevation of temperature, at least he does not refer to it, while the property of elevating the temperature seems to be the most characteristic effect of the Iron Mountain water poison. Typhotoxine produced profuse diarrhœa; while the other poison has shown no such effect. It may be remarked here that the fever at Iron Mountain has been characterized by the existence of constipation in the majority of the cases.

However, these differences in physiological action may be due to the fact that different animals were used, guinea pigs in one case, and cats in the other.

In 1880, Eberth[2] first described an oval bacillus, which he had found in the spleen and mesenteric glands of persons dead of typhoid fever, and which is now generally believed to be the true germ of this disease. Before Eberth, Koch had observed this germ and had taken micro-photographs of it. Even before Koch, Browicz[3], Sokoloff[4], Fischel[5] and others had individually observed, in the tissues of typhoid subjects, oval bacilli, which were probably identical with those of Eberth and Koch.

These bacilli are about one third as large as the red blood-corpuscles of man, and about three times as long as broad, though they may grow to long threads. The short rods have plainly rounded ends, and very active movements. They are affected by the amaline colors less than most germs, and are best stained by methylimblue. Whether or not this germ produces spores is a question of much interest to bacteriologists. Gafky[6] found that in po-

[1] Weitere Untersuchungen über Ptomaine.
[2] Virchow's Archiv, B. 81 and 83.
[3] Birch-Hirschfeld's Lehrbuch der pathologische Anatomie.
[4] Virchow's Archiv, B. 66.
[5] Prager Medicinische Wochenshrift, 1878.
[6] Mittheilungen aus d. Kais. Gesundheitsamte, B. 2.

tato, gelatine and blood serum cultures, kept at the temperature of the body, spores were formed. This observation has been confirmed by Sternberg,[1] Flügge und Bolton[2], Vilchour[3], and Chantemesse and Vidal[4]; though on the other hand, Buchner[5], Seitz[6], Michael[7], and Frankel and Simmonds[8] have, after numerous investigations, been unable to detect any spore-formation. This question is also of interest to sanitarians, since germ-spores resist disinfectants, which destroy germs growing without spores. Very recently Birch-Hirschfield[9] has apparently settled this question by detecting the spores by growing the bacillus in stained cultures. Another point of interest to sanitarians is the capability of this germ to resist high and low temperatures. Prudden[10] found them capable of growth after having been frozen in ice for 103 days and after having been heated to 56° C. This confirms the belief of sanitarians in this country that typhoid fever may be induced by the use of impure ice. The same investigation showed that frequent, alternate freezing and thawing did destroy the germ.

Still another point of interest is the fact that this germ will grow in various media. Seitz[11], and Wolfhügel and Riedel[12] found that it grew abundantly in milk. In our experiments, as has been seen, we obtained the poisonous extract from both the milk and meat cultures, though it was more abundant in the latter. It is worthy of note that the milk culture became acid in reaction, a fact which has also been observed by Löffler[13]. Seitz found that while the bacillus grew in both acid and alkaline urine, its growth was more abundant in the latter. However, it is probably of no sanitary importance whether the germ be taken into the stomach in milk or in water, for, in either case, on reaching the small intestine, it will find an alkaline medium in which to multiply. Wolfhügel and Riedel found that the bacillus multiplied in water which had been boiled, when kept at 16° C. Balton found the "spores" in stagnant water a month and longer after the introduction of the germ. Hochstetter[14] found the germ in artificial seltzer water a week after its introduction. Seitz found that quinine, kairin, antipyrine, thalline, salicylic acid and calomel in certain proportions arrest the growth of the germ in cultures, but that naphthalline, which seems to be a useful intestinal disinfectant in some diseases, is without effect upon the typhoid bacillus.

Upon potatoes, the typhoid bacillus shows a characteristic growth. It forms a mould wholly invisible to the unaided eye. After three or four days, if kept at ordinary temperature, after two days if kept at the temperature of the body, the surface of the potato looks moist, but no other change is observable. If the surface be scraped with a sterilized needle and the material thus obtained be examined under a sufficient power, it will be found to consist of active, moving typhoid bacilli. By making potato cultures, this bacillus can be distinguished from all known germs. Indeed, the best bacteriologists regard the potato culture as the crucial test for the

[1] Medical News, April, 1887.
[2] Zeitschrift für Hygiene, B. 1.
[3] Lancet, 1886.
[4] Archives de Physiologie. 1887.
[5] Archiv für Hygiene, B. 3.
[6] Bacteriologische Studien zür Typhusätiologie, 1886.
[7] Fortschritte der Medicine, 1886.
[8] Du ätiologische Bedeutung des Typhusbacillus, 1886.
[9] Archiv für Hygiene, B. 7.
[10] Medical Record, 1887.
[11] L. C.
[12] Arbeiten aus dem Kais. Gesundheits amte, B. 1.
[13] Berliner klinische wochenschrift, 1887.
[14] Centralblatt für Bakteriologie und Parasitenkunde, B. 1.

typhoid bacillus, and this test must always be made before one can be certain that he has this germ.

That the Iron Mountain water contained the typhoid bacillus was demonstrated by the potato culture and by microscopical examination, as well as by a physiological experiment. The first cultures were made as has been stated, Nov. 9, about two weeks after the water had been received. These cultures contained, besides the typhoid bacillus, germs ordinarily found in water; but the second cultures, made Dec. 7, contained only the typhoid bacillus. These had either destroyed or outlived the non-pathogenic organisms. This is an interesting fact, since it shows the poisonous germ to be very tenacious of life. Moreover, this observation is at variance with that of Kraus,[1] who found that the ordinary water bacteria destroyed the typhoid bacillus, though this difference may be due to the different temperatures at which the water was kept. Kraus kept the water in his experiment at 10½° C., while the Iron Mountain water was kept in a jug, in a basement room, the temperature of which was about 20° C.

In the meat peptone preparation the bacillus formed a scum, which had the lustre of mother of pearl and was bluish-gray, becoming slightly brownish after some weeks. Some of this growth was removed with a sterilized rod, rubbed up with 2 c. c. of water, which had been boiled, taken into a large, sterilized hypodermic syringe and injected into the abdominal cavity of a cat. Before the injection the hair was cut from the abdomen at the place of injection, and the skin was washed first with absolute alcohol and then with a one-half per cent solution of mercuric chloride. The injection was made at 2:25 P. M., Dec. 20. The temperature of the cat, taken in the rectum, before the injection was 101.5°. Twenty minutes after the injection, there was a fecal movement, and a few moments later, the animal vomited. The vomiting was repeated four or five times during the afternoon. When not vomiting or attempting to do so, the animal seemed greatly prostrated. She rested on her abdomen with her chin upon the floor and could not be easily aroused. She made several attempts at stool, but there was no purging or diarrhœa.

Dec. 21, 7:45 A. M.—The cat still lies in the same position. She refuses food. The temperature in the rectum is 96.4°.

2:30 P. M.—Cat still lies upon the floor and refuses milk. Temperature, 98.5°.

4:20 P. M.—Temperature, 101.4°.

5:30 P. M.—Temperature, 101.8°.

Dec. 22, 8:00 A. M.—Cat seems some better, but refuses food, and is very weak. She is unable to cry aloud; temperature, 103°.

2:30 P. M.—Takes some milk; temperature, 104°.

4:20 P. M.—Temperature, 104.4°.

Dec. 23.—The cat seems to be recovering rapidly. She takes food greedily and the temperature is normal.

The animal was then killed with chloroform. There was nothing abnormal at the point of injection. Nothing abnormal could be found in the peritoneal cavity. No trace of the small masses of injected bacilli could be found. The mucous membrane of the small intestines was slightly hyperæmic and in the region of Peyer's glands were observed four little ulcerations about the size of a pin head. Two or three similar ones were found in

[1] Archiv für hygiene, B. 6.

the ascending colon, but one of these was about four times as large as those in the small intestines, and around this was quite an area marked by inflammatory action. Careful inspection of all the abdominal and thoracic organs failed to reveal any further abnormality.

This result was very satisfactory, and leaves no room for doubt concerning the existence of the specific poison of typhoid fever in the Iron Mountain water.

It is to be noted that the lower animals are not subject to long-continued typhoid fever as is man, and a temporary effect from which the animal would within a few days die or recover is all that can be expected. Besides, the lessons in our experiment were certainly satisfactory. We hope to repeat this experiment several times.

It will be interesting to know something about the sanitary condition of Iron Mountain. For our information upon this point we are wholly indebted to Drs. J. A. Crowell and G. B. Johnson, physicians to the Chapin mine, who have been kind enough to answer our numerous inquiries.

Iron Mountain is a village with a permanent population of about 4,800, and during the summer months this number is augmented by some 2,000 floating population. As there are only about 1,000 buildings all told, and as some of the dwellings are very small, the village is very much crowded. The village is situated in a valley, the lowest portion of which was once a swamp, extending north and south. Upon each side the hills are steep and portions of the village lie upon these hillsides. The soil is drift of sand and gravel except in the lowest portions of the valley, where the drift is overlaid with vegetable mould. The depth of the drift is very variable. In some places the ledge of rock, which is of the Huronian strata, outcrops on the hilltops, in others on the hillsides, and in others in the valley. The ledge stands nearly on edge, dipping at from 70° to 80° to the north. The drift is so porous that within twenty-four hours after heavy rains the surface becomes dry.

A portion of the village, about 300 houses, has a system of water-supply, the source of which is a shaft 40 feet deep and far away from any source of contamination. An analysis of this water by Messrs. Brewster and Brown, chemists to the Chapin mine, shows the following:

Free ammonia, parts per million	0.02
Albuminoid ammonia, parts per million	0.05
Chlorine, grains per gallon	0.4
Calcium carbonate, grains per gallon	10.476
Magnesium carbonate, grains per gallon	5.324

Dr. Crowell writes: "Those drinking this water have been almost wholly exempt from the fever, and yet there have been some remarkable exceptions, a whole family coming down, while all neighbors were free from any sickness, and all drinking of this water."

The remaining portion of the village, the part in which the fever prevailed, derives its drinking water from wells sunk from six to twenty feet. There are no sewers or other means of removing filth. Privy vaults are used, and slops and garbage are thrown out in back yards and streets. During the past summer, a most disagreeable odor of decomposing matter greeted one in passing along the street. There is a ditch running through the village, which conveys the water from the mine to a small lake beyond

the village. This ditch, quite naturally, is used by many as an open sewer, and the ice supplied the village last summer was taken from this small lake into which the ditch empties.

Dr. Johnson writes that the outbreak of typhoid fever appeared early in August, following a severe epidemic of dysentery. Up to Dec. 21, he knew of 350 cases, about ten per cent of which had terminated fatally. The later cases, however, are much more malignant than those which occurred during the summer and early fall. Persons have presented themselves daily at the office for a week, complaining of pain in head, chest and back, loss of appetite and distressing feeling of languor, but have shown no elevation of temperature; then, within twenty-four hours, the temperature will be up to 104° or 105°. Diarrhœa was not present in the majority of the cases; indeed, constipation was more frequently the source of trouble.

The well (known as the Davis well) from which the water was taken which was sent to us, is sixteen feet deep. It is situated under the house and is forty feet from the stables and privy. Thirteen of the inmates of the house had the fever. (The doctors have failed to inform us of the total number occupying the house or using the water.)

An analysis of the water by Messrs. Brewster and Brown shows the following:

Free ammonia, parts per million, 2.27.

Albuminoid ammonia, parts per million, 0.26.

Chlorine, grains per gallon, 8.00.

These figures give unquestionable proof that the water is contaminated with animal excretions.

Manning's well, situated just across the street from the Davis well, is a drive well, carried down into the rock, and furnishes a fairly good water, notwithstanding the fact that surroundings are bad. Brewster and Brown give the following results of their analysis of this water:

Free ammonia, parts per million, 0.017.

Albuminoid ammonia, parts per million, 0.070.

Chlorine, grains per gallon, 0.050.

Dr. Crowell informs us that it has been decided to supply the village with water from some springs, the analysis of which show the following figures:

Free ammonia, parts per million, 0.032.

Albuminoid ammonia, parts per million, 0.039.

Chlorine, grains per gallon, 0.10.

Calcium carbonate, grains per gallon, 5.090.

Magnesium carbonate, grains per gallon, 3.558.

There can be no question about the need of a supply of pure water. This should by all means be obtained, and some provision should be made for disposing of excrement, slops and garbage. It matters not how cold it may be this winter, the low temperature will not destroy the typhoid germ unless there be successions of freezing and thawing. And with the soil filled with these germs some of them will be likely to find their way into the air breathed, food eaten or water drank, and produce the disease. It should also be remembered that typhoid fever may be caused by the use of impure ice.

Since writing the above, Dr. Crowell has furnished us with some additional facts of interest. "The fever was brought to the village by a man from a railroad construction camp. This man died a few days after his arrival. The symptoms were very variable. In some they were typical from

beginning to end, but in others they were very irregular. Constipation for the first ten days and frequently throughout the whole course of the disease existed in half the cases; and the abdominal symptoms, pain, tenderness, tympanitis, gurgling in the right iliac fossa, although certainly present in many cases, were conspicuously absent in a very large number. Intestinal hemorrhage occurred quite frequently and was the cause of death in one case in which we could never find any elevation of temperature. A subnormal temperature was very frequently observed, not only in the start, but throughout the disease. Failure of heart power, perforation, hemorrhage, pneumonia and meningitis, in the order named, were the causes of death. In only one case could we get an autopsy. It was one in which the symptoms were least like typhoid. The temperature was low, and there were no abdominal symptoms and no diarrhœa; yet the ilium was darkly congested, there were ulcerations of Peyer's patches, and, although no perforation could be seen, when the gut was inflated, it slowly collapsed."

In conclusion, we may state that there cannot be any doubt that the epidemic at Iron Mountain is one of genuine typhoid fever. The intestinal lesions were observed in the one post mortem. Similar lesions were found in the cat, the specific germ of typhoid fever exists in the water, and the chemical poison, or ptomaine, is formed by the growth of this germ.

It is well known that typhoid fever invariably follows dry seasons, and is coincident with low water in wells (see paper by the Secretary of the Michigan State Board of Health. Report for 1884, pp. 89–114.) There are, on an average, about one thousand deaths and ten thousand cases of sickness from this disease annually in Michigan. These figures can be greatly reduced if people will cease polluting the soil about their houses with slops, garbage, cesspools and privy vaults, and will see to it that their drinking water is pure beyond all question. When there is any doubt the water should be boiled, but it should be remembered that, while the typhoid germ most frequently finds its way into the body with the drinking water, it may be taken in with any food, and even with the air. When a case of typhoid fever occurs, all discharges should be thoroughly disinfected, and the earth, water and air about our homes must be pure, if we escape this disease altogether.

FOUR CASES OF POISONING FROM TYROTOXICON, WITH THREE FATAL RESULTS.*

INVESTIGATIONS AS TO THE ORIGIN OF THE POISON; RESULTS OF THE AUTOPSY AND CHEMICAL ANALYSES.

BY VICTOR C. VAUGHAN, M. D., PH. D.

September 23, 1887, I was visited by Dr. A. G. Mesic, of Milan, Michigan, who informed me that he had four members of a family under his charge, all of whom were seriously ill with peculiar symptoms, which he believed to be caused by tyrotoxicon. Since Dr. Mesic has written out for me the history of these cases, I will insert his report in full, as follows:

"Saturday, September 17, while passing the residence of S. H. Evans, a respectable farmer, I was called in to see him. I found him—a man of about fifty years, spare and muscular—vomiting severely, with flushed face, but with a temperature of 96° F. There was marked throbbing of the abdominal aorta; the tongue had a white, heavy coating, and the breathing was very labored. I set to work with the ordinary remedies to allay the vomiting, which had already continued for some hours. The vomited matters were colored with bile. Pupils were dilated, and a rash resembling that of scarlatina, but coarser, covered the chest, forearms, and legs below the knees, while the abdomen and thighs remained unaffected. As the bowels had not been moved since the beginning of the attack, I administered a purgative dose of calomel with a little podophyllin and rhubarb. On Sunday a small stool resulted. During that day and night, and the following day, the retching and vomiting continued. Small doses of carbolic acid seemed to give the most relief. After the movement of the bowels the symptoms were somewhat more promising; but a heavy and unfavorable stupor was observable and persistent.

"On Sunday the coating of the tongue remained very thick, and had changed to a dark brown color. At first I thought that his symptoms indicated a depressed condition, which I had known in one instance to precede typhoid fever. However, after a few days, I concluded that I must look for the cause of the condition among the poisons; but I could think of no one

*These cases were reported verbally to the State Board of Health at its meeting Oct. 11, 1887, and an abstract of Dr. Vaughan's report was printed in the pamphlet proceedings of that meeting. A vote of thanks was tendered to Dr. Vaughan, and he was asked to prepare a full report for publication in the Annual Report. This paper was published in the Medical News of Dec. 3, 1887. It is part of the First Quarterly Report of Work in the Michigan State Laboratory of Hygiene at the State University. H. B. B., Sec. S. B. of H.

poison which would be likely to produce all the symptoms observed. During Monday, Tuesday, and Wednesday there was but little change, and the treatment was continued.

"On Thursday morning I found the son Arthur, a lad of eighteen years, strong and vigorous, suffering with the same symptoms, only in a more violent form. After supper on Wednesday evening, he was taken with nausea and vomiting. He had no rash, but the symptoms were otherwise identical with those of the father, except in being more severe. I gave a cathartic, which acted only slightly.

"At my evening visit I found Mrs. Evans, a lady of about forty-five, previously in good health, with the same symptoms. In this case the stupor was more marked from the first. I was unable at any time to obtain any cathartic action in this case. Copious enemata of warm water were used, but succeeded only in washing some hardened lumps from the rectum. By this time I had concluded that the poison was most likely tyrotoxicon.

"On Friday morning the only remaining member of the family at home, Miss Alma, sixteen years of age, was affected in the same way as the others. On that day I went to Ann Arbor, and gave a history of the cases so far to Dr. Vaughan, who, from the symptoms, thought that my diagnosis was most probably correct, and he advised with me as to treatment, which I carried out. I gave two grains of sodium salicylate every four hours, and used small doses of the tonics and stimulants, quinine, nux vomica, digitalis, whiskey, and the aromatic spirits of ammonia. On Saturday the symptoms in all remained unimproved, and in the mother and son the stupor and labored breathing grew more marked.

"On Sunday, I again went to Ann Arbor, and brought Dr. Vaughan with me to see the patients. The temperature of the mother on Sunday was as low as 94°, and that of the son 95°. Dr. Vaughan agreed with me as to diagnosis and treatment. Sunday evening the patients were all removed to the house of a neighbor, about forty rods distant (the reasons for this will be given later). Dr. Vaughan and I both expressed the fear that the mother, and possibly the son, would not live through the night. Both of these rapidly grew worse, and the son died at 7:45 A. M., and the mother at 4 P. M., Monday.

"During Monday the daughter rapidly grew worse, and at the time of her mother's death could not be aroused, and practically she remained unconscious from that time on. The father was very weak, but retained his consciousness all the time. Convulsive movements of the limbs had been noticed in the son, but not in the mother. These now became more marked in the daughter, who remained in the heavy stupor, with labored breathing, until 5 P. M. Thursday, when she died.

"Mr. Evans has slowly improved, and now, October 18, is able to walk about the room. The sodium salicylate, even in the small doses used, seemed to cause severe headache; so apparent was this that the drug was discontinued, and drop doses of amyl nitrite, given every hour, seemed to relieve the pain in the head. The father's temperature remained below the normal until Thursday, October 14, when it reached the normal. After this it was found once as high as 99.5°, then 99°, then again normal, where it remains.

"All complained of a burning constriction in the throat, and difficulty in swallowing, and all, as long as they were conscious, frequently called for ice.

In all the pulse was rapid and feeble, and death seemed to result from failure of the heart. Those who died voided urine involuntarily, while Mr. Evans passed small quantities frequently, and for this some buchu and uva ursa were given. During his convalescence some small doses of morphine were given to the father, as he was unable to sleep, and became very restless. He is now taking teaspoonful doses of the elixir of calisaya and iron every four hours."

As stated above by Dr. Mesic, I first saw these patients Sunday, September 25. On a sofa in the room we found the daughter, Alma. She had been vomiting during the day, and seemed much exhausted. She was not inclined to talk, and seemed to be in a stupor, though when spoken to, she responded rationally. Her pupils were slightly dilated, her tongue coated, her pulse 120 and weak, her face flushed, and a violent throbbing could be felt over the abdomen, which was retracted. Her temperature was 96°.

In another room were the father, mother, and son, two of them dying. The father was rational, and talked with some freedom when I asked as to the kind of food they had been eating, etc. His pupils were normal. His face could not be said to present any peculiar feature. His pulse was rapid, breathing somewhat labored, and the throbbing of the abdominal aorta was plainly felt. The abdomen was retracted, and there was no pain on pressure. He complained of a burning constriction of the throat, swallowed with difficulty, and said that his throat and stomach felt as though they were on fire.

The mother lay perfectly still with eyelids closed, as if in a deep sleep. Her pulse was rapid, her face had a livid flush, her breathing was about 35 per minute, and labored. The skin was cool, but neither abnormally moist nor specially dry and harsh. She could not be aroused. In fact, she was comatose.

The son rolled uneasily from one side of the bed to the other. His breathing, also, was very labored. His eyelids were closed, and the pupils were markedly dilated—did not respond to light. He could not be aroused. In mother and son, as well as in father and daughter, the abdomen was retracted, and the throbbing of the abdominal aorta was easily felt.

Now, to what were these symptoms due? They were certainly those of some poison. Dr. Mesic had brought me some of the vomited matter, which I tested thoroughly for mineral poisons, with negative results. The symptoms certainly were not those of morphine, strychnine, digitalis, or aconite. They did have some resemblance to those of belladonna, but yet they were not the symptoms of belladonna. The pupils were not as widely dilated as they would be in belladonna poisoning. There was in none of these persons the active delirium of belladonna poisoning. There was no picking at the clothing, no grasping of imaginary objects in the air, no hallucinations of vision. Surely it could not be any vegetable alkaloid with which I was familiar.

On the other hand, we know that nausea, vomiting, headache, dilatation of the pupil, rapid pulse, heavy breathing, constipation, and great prostration, with stupor, do occur in cases of poisoning with certain ptomaines. Therefore, we began to look for conditions which would be favorable for the production of putrefactive alkaloids. These conditions we were not long in finding.

The family, which consisted of the four persons sick, and of a daughter,

about twenty years of age, who was away from home at the time when the others were taken ill, and for some months before that time, was evidently a tidy one. This was shown by their personal appearance, and by the clothing and bedding. But the house in which they lived was very old and very much decayed. Mr. Evans had purchased the farm six years ago, and for some three years past, at least, they had been troubled every now and then, one or more of the family, with nausea and vomiting, followed by more or less prostration. But in no instance, up to the present illness, had the symptoms been sufficient to cause them to summon a physician. The family had worked hard in order to pay for the farm, and had determined to make the old house do until they were out of debt. Even before this family had moved to the farm, the house had been known among the neighbors as an unhealthy one, and there had been much sickness and a number of deaths among its former tenants.

The house is a frame one, and one of the neighbors said to me that it was an old house when he came to the neighborhood thirty-seven years ago. It consists of two rooms on the ground-floor, with attic rooms above. The frame rests upon four large logs or sills, which lay directly upon the ground, and are thoroughly rotten. There is no cellar under any part of the house. From the front, at least, the surface slopes toward the house, and the rain water runs under it. In the floor of one room a trap door had been placed, and directly under this a small excavation had been made for the purpose of collecting the rain water when it accumulated under the house. Although this pit was dry at the time of our examination, its sides and bottom were marked with cray-fish holes, showing that water had stood in it. The floor was laid of unjointed boards, and every time that it was swept much of the filth fell through the cracks, and every time that the tidy housewife scoured and mopped the floor, the water, carrying with it the filth, ran through the crevices, and thus the conditions most favorable for putrefactive changes were brought into existence, and maintained.

One corner of one of the rooms had been transformed into a small room, or buttery, as it was called, and in this, on shelves, the food was kept. On account of the more frequent scouring demanded by that part of the floor enclosed in this buttery, the boards had rotted away, and a second layer of boards had been placed over the original floor. Between these two floors we found a great mass of moist, decomposing matter, the accumulations of years, which the broom could not reach. When this floor was taken up a peculiar, nauseating odor was observable, and was sufficient to produce nausea and vomiting in one of the persons engaged in the examination. Some of the dirt from beneath the floor, and some of that which had accumulated between the boards in the buttery was taken for further study.

The condition of the house was supposed to be unfavorable to the patients, and for this reason they were moved, as Dr. Mesic has stated, to the house of a neighbor. Of course, thorough examination of the house was not made until the patients had been removed.

Special inquiry was now made concerning the food used by this family. They had been living very simply. They lived upon bread, butter, milk, and potatoes, with coffee and ripe fruit. They had eaten no canned foods for months. They ate but little meat. Occasionally a chicken was killed and served, and rarely some fresh meat was obtained from the village. During the week in which they were taken ill, all the meat used consisted of

slices from a piece of bacon, the only meat which was kept in the house, and a chicken. None of the latter remained, but the bacon was examined. It seemed in perfect conditon and contained no trichinæ. Moreover, as has been seen from the history of the cases, all the members of the family were not made sick by any one meal, but the opportunity of obtaining the poison must have been present for some time. Moreover, the fact that previous similar, but less severe attacks had occurred at intervals for the past three years convinced us that the poison must owe its origin to some long existing condition.

The drinking water supply was also investigated. The water was obtained from a shallow well, and some of it was taken for analysis. But several families had for years used water from this well, and had remained healthy.

The milk used by the family was studied. Of course, we could get none of that which had been used before the members of the family were stricken down. As soon as he made the diagnosis of tyrotoxicon poisoning, Dr. Mesic ordered the discontinuance of the use of milk, not only with the sick, but he forbade the daughter, who had returned, and any of the visitors using it. Mr. Evans owned four milch cows and they were supplied with fair pasturage and abundant water. The greater part of the milk was placed in tin cans, which were set in a wooden trough in the yard, and surrounded by cold water. The covers to the cans were arranged so that the air could have free access to the milk, and were left in this position until the milk was thoroughly cooled. Indeed, the cans were furnished by a creamery company, which followed the directions which I have previously given for the care of milk. On his first visit to me, Dr. Mesic brought some of the milk from one of these cans. This I examined, but failed to find tyrotoxicon in it.

However, the family did not drink any of the milk from the cans. That which they did use was kept in the buttery which I have described. Here it stood upon a shelf and some members of the family at least were in the habit of drinking from it between meals. This was especially true, it is said, of the son. He would frequently come from his work in the fields, go into the buttery and drink a glass or more of the milk. Mr. Evans states that he frequently observed that the taste of the milk was not pleasant. On my first visit to the premises, I advised that some milk should be taken from the cans, allowed to stand in the buttery over night and be sent to me the next day. This was done, and in this milk we found tyrotoxicon not only by the employment of chemical tests, but by poisoning a kitten with it.

On the death of the mother and son, Dr. Mesic asked for a post-mortem, but the friends objected, and the undertaker used an arsenical embalming fluid, so that, although consent was subsequently obtained, it was decided that the examination would be so vitiated as to be worthless. On the death of the daughter, Dr. O. C. Jenkins, the coroner, summoned a jury and held an inquest. The post-mortem was conducted by Dr. George A. Hendricks, in the presence of the jury and several physicians who had been invited. Dr. Hendricks has kindly furnished me with his report, which I present here in full:

The "autopsy was held fifteen hours after death. The abdominal viscera were first examined. The great omentum was small, in normal position, covering the small intestine. The small intestine was moderately distended with flatus. The jejunum was ashy-green in color; the ileum purplish-green. About eighteen inches from the termination of the ileum was found a diver-

ticulum two inches in length. The small intestine contained very little alimentary matter. The vermiform appendix was free, contained some small fecal lumps, and showed no evidence of any inflammation. The cæcum, ascending, transverse, and descending colon, were empty and their circular fibres were tightly constricted, except at intervals where the intestine was distended with gas. The sigmoid flexure was moderately distended with gas, and the rectum contained small bits of fecal matter. The stomach was somewhat contracted and lay wholly upon the left side of the median line. It contained a few ounces of fluid. Its extremities were ligated and the organ removed. The mucous membrane of the stomach and intestine were not examined until they reached the chemist. The duodenum was distended with flatus. The liver was normal in size and appearance. The gall-bladder contained about one ounce of bile. The spleen was normal. One-half ounce of fluid deeply stained with blood was found in Douglas' cul-de-sac. The uterus, Fallopian tubes, and ovaries were deeply congested. The left ovary was enlarged and presented on its posterior surface a hemorrhagic spot, oval, about one-half line in length, and several other less distinct ones. The right ovary was normal in size and showed numerous Graaffian scars. The ureters and bladder were normal; the latter contained a small amount of urine. The peritoneum, pancreas, and kidneys, were perfectly normal.

"The thoracic cavity was next opened. The lungs were normal; there was about one-half ounce of free serum in the left pleural cavity; none in the right. Pericardium normal; right auricle in diastole; left auricle and both ventricles in systole.

The dura mater showed venous congestion;" the arachnoid normal; the pia-mater congested. On the surface of the centrum ovale, small drops of blood oozed from the divided vessels. The large veins of the velum interpositum were distended. Third and fourth ventricles were slightly distended with serous fluid, but the walls were normal. There seemed to be slight softening of the optic thalami. The sub-arachnoid fluid was about twice the normal quantity.

On examination of the mucous membrane of the stomach and intestine in the presence of the chemist, Prof. A. B. Prescott, nothing abnormal could be found. The membrane was stained with bile, but there was not the slightest redness. The solitary glands were distinct but not at all inflamed. Peyer's patches were normal.

It will be seen that there existed no lesion which would account for the death. The venous congestion observed in the brain would follow from failure of the heart.

Some of the post-mortem appearances bore a striking resemblance to those which I had observed in cats poisoned with tyrotoxicon. This was especially noticeable in the condition of the mucous membrane of the stomach and intestine. Tyrotoxicon produces the symptoms of a gastro-intestinal irritant, but not the lesions. The contraction of the circular fibres of the intestine, which undoubtedly caused the constipation, I had also observed in cats that died from tyrotoxicon poisoning without either vomiting or stool. The action of this poison upon the stomach and intestines must be through the nervous system. Small doses cause both vomiting and purging, while, after large doses, vomiting may be impossible, and obstinate constipation may exist. Both the vomiting and purging after small doses are undoubtedly due in part to increased activity of the circular fibres of the muscular coats, induced

through the nerves; and the inability to vomit, and the constipation, one or both of which may be observed after large doses of the poison, are due to spasm of the same muscles, induced in the same manner.

Prof. A. B. Prescott was requested by Coroner Jenkins to analyze the material for mineral and vegetable poisons. He made analyses of the stomach and part of its contents, and a portion of the liver. His results were wholly negative.

Mr. F. G. Novy tested a cold-water extract of the finely divided intestine for ptomaines. The fluid, which was acid in reaction, was filtered, then neutralized with sodium bicarbonate, and shaken with ether. The ether, after separation, was removed and allowed to evaporate spontaneously. The residue was dissolved in water, and extracted again with ether. This ether residue gave the chemical reactions for tyrotoxicon, and a portion of it was administered to a kitten about two months old. Within half an hour after the administration the kitten began to retch, and soon it vomited. Within the next three hours it was noticed to vomit as many as five times. The breathing became rapid and labored. The animal sat with its head down, and seemed greatly prostrated. The pupils were examined, but could not be said to be dilated. There was no purging. The retching and heavy breathing, with evidences of prostration, continued more or less marked for two days, after which the animal slowly improved.

A quantity of fresh milk was divided into five portions of one quart each, placed in quart bottles which had been thoroughly cleansed, and treated in the following manner:

No. 1 consisted of the milk only, and was employed as a control test.

No. 2 was mixed with a drachm of vomited matter.

No. 3 was treated with a portion of the contents of the stomach.

No. 4 was treated with an aqueous extract of the intestine.

No. 5 was treated with a small portion of the soil, which had been taken from the floor of the buttery, stirred up with water.

These bottles were placed in an air-bath, and kept at a temperature of from 25° to 30° C. for twenty-four hours. Then each was tested for ptomaines. No. 1 yielded no tyrotoxicon, while all of the others contained this poison. The tests were both chemical and physiological. All of the samples yielded a non-poisonous base when treated according to Brieger's method, and the same substance was obtained from perfectly fresh milk. It is most probably formed by the action of the heat and reagents employed in this method. This base was obtained in crystalline form, and several portions of it were administered to kittens without any effect. The further study of this body will be of interest to toxicologists, because it gives many of the general alkaloidal reactions. At first we supposed it to be Brieger's neuridin, and this supposition may still be correct, but, as we obtained it, it gave some reactions which are not given by neuridin. Further investigations will be made on this point.

Tyrotoxicon was obtained from the filtered milk by two methods: (1) The one which we have previously used, and which consists in neutralizing the filtered milk with sodium bicarbonate, and extracting with ether. That portion of the poison employed in the physiological tests was obtained in this way, and in order to be sure that no poison came from the ether, the extract from the milk to which nothing had been added was given to a kitten, and was found to produce no effect. (2) The filtrate firom the milk was heated

to 70° C. (158° F. (tyrotoxicon decomposes at 91° C.) (195.8° F.)) for some minutes, and filtered. This filtrate, which was perfectly clear, was treated with a small quantity of nitric acid in order to convert the tyrotoxicon into a nitrate, then pure potassium hydrate in the solid form was added until the solution was strongly alkaline. This solution was concentrated so far as it could be, on the water-bath. (The potassium compound of tyrotoxicon is not decomposed below 130° C. (234 F.)) The dark brown residue, after cooling, was examined with the microscope and found to contain the crystalline plates of tyrotoxicon-potassium hydrate, along with the prisms of potassium nitrate. The former was separated from the latter by extraction with absolute alcohol and filtration. The alcohol was evaporated to dryness on the water-bath, and the residue again extracted with absolute alcohol. From this alcoholic solution tyrotoxicon was precipitated with ether. The precipitate was decomposed by adding acetic acid and heating, the tyrotoxicon being broken up into nitrogen and phenol. The phenol was recognized by precipitation with bromine water, and by other well-known tests.

On October 8th, the coroner's inquest, which had been adjourned after the *post-mortem*, in order to await the results of the analysis, was resumed, and after hearing the testimony in accordance with the above stated facts, the jury returned a verdict of death from poisoning with tyrotoxicon.

Ehrhart has recently published the history of some cases of poisoning from cheese, of which the following is an abstract: The family of a workman, consisting of eight persons, ate for supper 600 grammes (about 18 ounces) of Limburger cheese. The rind was covered with a heavy mould, while the interior had become fluid from putrefaction, and was of bitter taste. Three ate only of the mouldy rind, and these remained well. The next morning, the five who had eaten of the inner portion suffered from vertigo, nausea, vomiting, and abdominal pains; no stool. The father had convulsive movements of all the extremities. The pupils were dilated, and did not respond to light; there were double vision, cold sweat, skin cyanotic, abdomen distended, difficulty in swallowing, delirium, mild trismus, and temperature 40° C. (104° F.). The temperature of the mother, on account of the great collapse, was sub-normal. She had no convulsive movements, but there was prolonged loss of consciousness. The pulse was small and thready, and threatened paralysis of the heart. Recovery was very slow. The others suffered only from gastro-enteric symptoms. Ehrhart discussed the question as to whether these symptoms were due to tyrotoxicon, or to infection with micro-organisms; but as I have not had access to his original paper, I do not know what his conclusions are. (*Schmidt's Jahrbücher*, B. 213, S. 248.) However, there cannot be much doubt that in those cases in which the organism is taken into the alimentary canal, it continues the elaboration of its poisonous products.

There is one other point to which I will only refer at this time. It seems now that small doses of tyrotoxicon, especially when repeated, elevate the temperature. This is probably due to peripheral irritation, which is a common cause of elevation of temperature. On the other hand, fatal doses cause depression of temperature from collapse.

EXPOSURE OF THE STENOCARPINE FRAUD.*

BY P. G. NOVY, M. S.

In a paper published in the New York Medical Record, July 30, 1887, Dr. J. H. Claiborne, Jr., called attention to a new local anæsthetic which was said to have been obtained by Doctors Goodman and Seward from the leaves of a tree growing in Louisiana. Strange to say, neither of the two discoverers were able to name the tree which yielded this new alkaloid. Nevertheless, in order that the new base might not go unnamed, Dr. Seward dubbed it Stenocarpine, because of the likeness the tree bore to Acacia stenocarpa. This comparison was, as Dr. Hoffman at once remarked (RUNDSCHAU, Sept. 1887, p. 214), very suspicious, since A. stenocarpa is not an American plant, but is a native of Central Africa.

Dr. Claiborne's paper, detailing some experiments with this new alkaloid, was followed by another in the same journal (Aug. 13), from no less an authority than Prof. Knapp, of New York, who made some physiological experiments with the same substance. He arrived at the conclusion "that the new local anæsthetic is very similar to cocaine, chiefly differing from it by its more powerful and lasting mydriatic property." In a still more recent article Dr. Claiborne (Med. Record, Oct. 1), announced the source of the new alkaloid to be the Gleditschia triacanthos, Linn., also at first indicated by Dr. Hoffman. Another peculiar thing was, that neither Goodman nor Seward had in their possession any specimen of the leaves from which they had extracted their alkaloid. At Dr. Claiborne's request Mr. Goodman wrote to Louisiana for some of the leaves. After some delay, a batch of leaves was received which did not appear to be identical with those from which the anæsthetic principle had been obtained. Accordingly more explicit directions were sent, and this time the genuine leaves were received and identified as those of Gleditschia. The reason which they assigned for not having any of the leaves in their possession was that they had reduced the active principle on the banks of the Mississippi, and then brought it to New York.

It is pertinent to observe at this point that no communication has been made as to the chemical properties of this new substance, although Dr. Seward is reported as having analyzed the leaves and isolated from them the

*A paper similar to this, but having a different title, was published in the Pharmaceutische Rundschau, for November, 1887.

The solution of which this report treats, consisted of a mixture which contained a dangerous quantity of cocaine, and was advertised as a perfectly safe preparation from the honey locust. It was treated of popularly by the newspapers before its exposure, and all classes were more or less interested in it. The exposure was so complete that the preparation was driven from the market. If the purity of medicine is of value to public health, certainly this exposure is.

active principle, which was found to be an alkaloid. Beyond this mere mention, and the statement made by Mr. Goodman that "the new alkaloid is not, strictly speaking, a powder, but a semi-liquid mass, of a greenish tint," no further communications can be found. Inasmuch as the salt was said not to be permanent, a two per cent solution was recommended. An ounce of this solution cost $6.00, which would give sixty cents as the cost per grain. It is, therefore, all the more surprising that such well-informed and experienced physicians as Dr. Knapp and Dr. Claiborne should give full credence, without stopping to ask for positive proofs, as to the individuality and genuineness of this substance.

At the request of Messrs. Lehn and Fink I examined what was labeled as a "two per cent solution of the so-called Gleditschine or Stenocarpine," and the results obtained deserve the attention of all those interested in "new and wonderful remedies."

The solution was light yellow in color, acid in reaction, and possessed a sweetish odor, strongly resembling that of liquorice.

An examination for inorganic acids showed the presence of hydrochloric acid and a small quantity of sulphuric acid.

A definite quantity of the liquid was acidulated with hydrochloric acid and extracted with ether. The residue obtained on evaporation of the ether was colorless and crystalline and corresponded to 0.31 per cent. It possessed a strong "Fine-cut" like odor and was found to be Salicylic acid. Fe_2Cl_6 and $PtCl_4$ gave the characteristic pink to violet color with solutions of the residue. It may be well to remark here that the latter reagent, $PtCl_4$, is equally as good as Fe_2Cl_6 in testing for salicylic acid. The color reaction in both cases is almost identical.

The acid aqueous solution containing the alkaloid was now rendered alkaline with NH_4OH, and again extracted with ether. The addition of the alkali produced a heavy white precipitate which dissolved readily in ether. The clear ether solution on spontaneous evaporation left a colorless crystalline residue possessing the characteristic odor of cocaine. It gave an alkaline reaction with moist litmus paper. The solution of its hydrochloride gave with ordinary and with alkaloidal reagents reactions identical with those of cocaine. The free alkaloid, when recrystallizing in a glass dish, formed at first a colorless syrup, which gradually became crystalline. Cocaine very often shows the same behavior. The syrup as well as the crystals possessed a bitter taste, and produced a strong flow of saliva and a benumbing effect on the tongue. The crystals melted at 89° C.

A small portion of the alkaloid was heated with a few drops of nitric acid for a few minutes and then gently evaporated to dryness. The cold residue touched with a few drops of alcoholic solution of KOH developed a beautiful violet color, and at the same time a strong odor of methyl benzoic esther. This color reaction is characteristic of the atropine group of alkaloids. It is well to note at this point that, when cocaine is treated in the same manner, no color reaction is obtained, but the characteristic odor of benzoic esther (similar to Oil of Wintergreen) is always produced on the final treatment with alcoholic solution of potash. Minute quantities of cocaine can thus be distinctly recognized. As a qualitative test for the presence of cocaine, it is perhaps the best that I am acquainted with.

Whilst speaking of cocaine, I desire to make note of the observation, numerous statements to the contrary, that chloroform does not readily extract

cocaine from alkaline solutions. In fact I have been unable, even on prolonged agitation with chloroform, to remove the precipitate of cocaine produced by addition of NH_4OH to solutions of its salts.

Two determinations were made of the amount of the free alkaloids present in the "*Gleditschine*"-solution. This was found to be 5.81 and 5.87 per cent.

The specimen, it will be remembered, was labeled as a 2 per cent solution of Gleditschine.

On the label, the formula $C_{20}H_{21}NO_3$ was ascribed to this new alkaloid. In order to more fully confirm the results given above, and at the same time to see what truth, if any, lay in the formula assigned, the alkaloidal residue was recrystallized several times from alcohol and from ether, and then subjected to ultimate analysis. The platinochloride was also made and the per cent of platinum determined. In the following table the results obtained are compared with the theoretical percentages calculated for cocaine, for atropine, and for "Gleditschine," $C_{20}H_{21}NO_3$.

	%C.	%H.	%Pt.
Found in the base extracted from the so-called Gleditschine solution	67.84	7.23	19.41
Calculated per cent:			
in Cocaine ($C_{17}H_{21}NO_4$)	67.33	6.93	19.14
in Atropine ($C_{17}H_{23}NO_3$)	70.06	7.96	19.70
in $C_{20}H_{21}NO_3$	74.30	6.50	18.43

The above results confirm most decidedly the conclusion already arrived at—namely, that the so-called Gleditschine or Stenocarpine is nothing but a mixture of cocaine and atropine.

In order to ascertain the amount of atropine present in the solution, the amount of H_2SO_4 was determined and found to be 0.073 per cent. This amount, calculated as atropine sulphate, gives 0.50 per cent of the latter salt. The per cent of atropine thus obtained was subtracted from the per cent of total alkaloids and the difference calculated as cocaine hydrochloride. This was found to correspond to 6.03 per cent.

The so-called Gleditschine or Stenocarpine consists, therefore, essentially of 6.00 per cent of Cocaine hydrochloride, 0.50 per cent of Atropine sulphate, and about a third of a per cent of Salicylic acid. The latter is used as a preservative.

Immediately after making my analysis of the solution of "Gleditschine," as reported above, I obtained two pounds of the perfectly fresh leaves from a hedge growing in Ann Arbor, and which Prof. Spaulding of the Chair of Botany pointed out to me as being Gleditschia triacanthos. These two pounds were subjected to chemical analysis. The leaves were thoroughly crushed in an iron mortar, then repeatedly extracted with a dilute alcohol 5 per cent solution of sulphuric acid. The concentrated percolate thus obtained was evaporated at a low temperature to drive off the alcohol. The aqueous solution was then filtered and the filtrate, after being made alkaline with ammonia, was thoroughly extracted with ether. The ether solution was agitated with a dilute aqueous solution of hydrochloric acid for the purpose of forming hydrochlorides of any alkaloids that might be present in the ether solution. The acid aqueous solution was now made alkaline with ammonia and extracted with ether. The ethereal solution on spontaneous evaporation left behind a scarcely perceptible residue which contained some

ammonium chloride. Applied to the clean mucous membrane it produced no anæsthetic effect whatever, though it seemed to me that a slight aconite like tingling was felt. The residue, dissolved in a few drops of dilute hydrochloric acid, gave the following reactions:

Iodine in potassium iodide, a brown precipitate much darker than that produced by either cocaine or the "Gleditschine" solution.

Picric acid, an abundant yellowish white precipitate.

Mayer's Reagent, a white precipitate.

Phospho-molybdic acid, a heavy white flocculent precipitate.

The remainder of the hydrochloric acid solution was evaporated to dryness on a water-bath, treated with a few drops of nitric acid and again evaporated to dryness. A drop of alcoholic potash added to the residue produced neither coloration nor any odor. This same test applied to the alkaloids from the "Gleditschine" solution gave a beautiful violet color and a strong odor of methyl benzoic esther.

These results then show that the leaves of Gleditschia triacanthos do not contain the alkaloid which they were reported to contain. Traces of an alkaloid were, however, found to be present, and these gave reactions different from the alkaloid of the "Gleditschine" solution. It will be well to add that the leaves of this tree have been examined a short time ago by B. H. Paul and A. J. Cownley (Pharm. Journ. and Trans. Oct. 15, p. 317); by Mr. Thompson of Parke, Davis & Co. (Medical Age, Oct. 25, p. 466) and by Prof. Karl Mohr of Mobile (Pharm. Rundschau, Nov. 1, p. 250), all of whom have obtained negative results.

Hygienic Laboratory, University of Michigan,
Ann Arbor, Nov. 9, 1887.